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THE
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Cancer research news for clinicians

Survival Benefit For Vinorelbine-Cisplatin In NSCLC Patient, Phase III Trial Finds

By Eric Lai

Vinorelbine-cisplatin drug combination used as adjuvant chemotherapy shows survival benefit in certain non-small cell lung cancer patients, according to final results of large randomized phase III trial presented at the World Conference on Lung Cancer, held in Barcelona, Spain, last month.

The study, known as ANITA, Phase III Adjuvant Vinorelbine and Cisplatin versus observation in completely resected (Stage I-III) Non small Cell Lung Cancer patients, was conducted by Rafael Rosell of the Catalan Institute of Oncology to evaluate the impact on survival of adjuvant vinorelbine-cisplatin

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Prostate Cancer:

NCI Phase II Trial Tests Vaccine Plus Hormone Therapy For Recurrent Prostate Cancer

A cancer vaccine combined with hormone-deprivation therapy can help patients with recurrence of prostate cancer, according to the results of a phase II trial led by scientists at the National Cancer Institute.

The results were published in the August issue of the Journal of Urology.

The trial was designed to treat patients with nonmetastatic prostate cancer who were experiencing rising levels of prostate-specific antigen, which can indicate recurrence of the disease. Prostate cancer often progresses several years after treatment with hormone-deprivation therapy.

This is the first study to combine antiandrogen therapy (reducing the amount of androgens, which are male sex hormones) and a cancer vaccine for treating prostate cancer, and also the first randomized clinical trial in this population of prostate cancer patients. Cancer vaccines are designed either to treat existing cancers or to prevent the development of cancer. The experimental vaccine used in this study was designed to strengthen the ody's natural defenses against prostate cancer.

"The question is, what do you do for someone who has already failed standard therapy with hormones?" said Philip Arlen, of NCI's Laboratory of Tumor Immunology and Biology. "This study was designed to answer that question and examined a population of patients whose cancers were resistant to hormone therapy, had no metastatic disease that was observable by computed tomography (CT or CAT) scan, but had a rising PSA score, an indicator of recurrence."

NCI scientists randomly assigned 42 prostate cancer patients to receive

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Top Abstracts Presented At World Lung Cancer Meeting

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compared to observation.

From December 1994 to December 2000, 840 patients (median age 59 years) were randomized to receive either four cycles of adjuvant vinorelbine-cisplatin (vinorelbine 30 mg/m^2/week for 16 consecutive weeks and cisplatin 100 mg/m^2 on d1 every 4 weeks) or observation. The ANITA study encompassed 101 centers in 14 countries. Patients were predominantly male (86%) and the percentage of patients with stage I, II and IIIA NSCLC were 35%, 30% and 35% respectively. The 407 patient group receiving vinorelbine-cisplatin and the 433 group solely being observed were well balanced in terms of age, gender, stage, histology and resection type.

Median survival was significantly different between the two groups after a median follow-up of greater than 70 months; 65.8 months for patients on vinorelbine-cisplatin versus 43.7 months for observation (p=0.0131). Two, five and seven-year survivals were 68%, 51% and 45% for vinorelbine-cisplatin patients versus 63%, 43% and 37% for observation patients.

Five-year survival for stage I, II and IIIA NSCLC patients were 62%, 52% and 42% for those on vinorelbine-cisplatin versus 63%, 39% and 26% for those being observed. Five patients (1%) died of drug-related toxicity, and the percentage of patients taking vinorelbine-cisplatin who experienced neutropenia, febrile neutropenia, nausea/vomiting, constipation or peripheral neuropathy was 86%, 8.5%, 27%, 5% and 3% respectively.

These results demonstrate that taking adjuvant vinorelbine-cisplatin significantly improves survival in completely resected stage II and IIIA NSCLC patients, but not in stage IB patients.

Other studies presented at the Presidential Symposium of the conference included the following:

Surgery Versus Thoracic Radiotherapy

Radical surgery following induction chemotherapy for stage IIIA-N2 non-small cell lung cancer doesn't improve either overall survival or progression-free survival when compared to thoracic radiotherapy, according to the results of a randomized trial.

Of the 570 patients with histological/cytological proven stage IIIA-N2 NSCLC who received three cycles of platinum-based induction chemotherapy, roughly 62% actually responded to the therapy, said Jan van Meerbeeck of University Hospital in Ghent, Belgium.

From the 62% who responded, 167 patients received radical surgery (radical resection with lymph node dissection and optional postoperative radiotherapy), and 165 patients were given thoracic radiotherapy (at least 40 Gy in 2 Gy daily fractions on the mediastinum with a boost to at least 60 Gy on the involved field). The primary endpoint was five-year overall survival. Secondary endpoints were progression-free survival and toxicity.

At a median follow-up of 72 months, median and five-year overall survival for radical surgery and thoracic radiotherapy patients were 16.4 versus 17.5 months, and 16% versus 13% respectively. Median and two-year progression-free survival rates for radical surgery and thoracic radiotherapy patients were 9 versus 11.3 months, and 27% versus 24% respectively.

Van Meerbeeck and his team did not find significant survival differences between using radical surgery or thoracic radiotherapy in stage IIIA-N2 NSCLC patients who respond to induction chemotherapy.

PET-CT Versus Remediastinoscopy

In a study performed by Paul De Leyn of University Hospitals Leuven in Belgium, the performance between two screening tools, remediastinoscopy versus PET-CT, was compared to see which is better at detecting residual mediastinal disease after induction chemotherapy for stage IIIA-N2 non-small cell lung cancer patients.

From April 2002 till December 2004, 24 patients underwent PET-CT, remediastinoscopy to biopsy all

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mediastinal nodal stations, thoracotomy with mediastinal nodal dissection, and attempted complete resection all after induction chemotherapy for mediastinoscopy-proven N2 NSCLC.

During the initial mediastinoscopy, the surgeon attempted to biopsy all accessible mediastinal nodal levels; all remediastinoscopies were performed using a videomediastinoscope by the same surgeon. Patients with positive (N2) remediastinoscopy underwent attempted complete resection.

PET-CT images were analyzed without knowledge of the surgical data and were scored positive for residual N2 disease when hypermetabolic mediastinal lymph nodes were present. The performance between the two tools was compared by a Fisher Exact test.

Out of the 24 patients included in the study, the thoracotomy of 17 patients (70.8%) showed that the subcarinal region was not adequately biopsied during remediastinoscopy. Remediastinoscopy was positive in 4 patients, and PET-CT showed positive mediastinal lymph nodes in 13 patients.

The sensitivity, specificity, and accuracy of remediastinoscopy were 28.6%, 100% and 58.3% respectively with a positive-predictive value of 100% and a negative-predictive value of 50%. These figures for PET-CT were 85.7%, 90% and 87.5% respectively with a PPV of 92.3% and a NPV of 81.8%. PET-CT had significantly better sensitivity (p=0.0032) and accuracy (p=0.0245).

De Leyn's study found that after a thorough initial mediastinoscopy, PET-CT proved to be far more accurate in the restaging of the mediastinum than remediastinoscopy, which had a relatively low sensitivity.

Phase III Study of Iressa

Nick Thatcher of Christie Hospital in Manchester, England, led a randomized phase III study to investigate the survival benefit of second-line and third-line gefitinib (Iressa) monotherapy in patients with advanced NSCLC. The trial was called ISEL, comparing Iressa and best supportive care to placebo plus best supportive care.

Participants had to have histologically/cytologically proven, locally advanced or metastatic NSCLC, at least one prior chemotherapy regimen, and had to be intolerant of or refractory to their most recent regimen. Out of the 1,692 qualified patients who were recruited from 210 centers in 28 countries, 1,129 patients received gefitinib (250 mg/day) plus best supportive care, while 563 patients received placebo plus BSC (both treatments given in a 2:1 ratio).

Disparities in terms of demography and disease characteristics were minimal between the two treatment arms. The primary endpoint was to observe the overall survival in both the overall population and in patients with adenocarcinoma; some secondary endpoints included time to treatment failure and objective response.

At median follow-up of 7 months, the median survival was 5.6 versus 5.1 months in the overall population (p=0.11), and 6.3 versus 5.4 months in patients with adenocarcinoma (p=0.07) for gefitinib and placebo respectively.

According to pre-planned subgroup analyses, gefitinib-treated patients with Oriental origin survived longer (median 9.5 months) than placebo-treated patients with Oriental origin (median 5.5 months), and gefitinib-treated patients who never smoked survived longer (median 8.9 months) than placebo-treated patients who never smoked (med. 6.1 months).

There were also statistically significant improvements in time to treatment failure and objective response for gefitinib as compared with placebo.

Thatcher concluded that the results from this study demonstrate that there is a difference between gefitinib and placebo in terms of survival, although this did not reach statistical significance in the overall or adenocarcinoma histology population. Subgroup analyses however suggested survival benefits in patients of Oriental origin and in patients who never smoked.

QOL In Lung Cancer Survivors

The quality of life of long-term lung cancer survivors is relatively unclear to most doctors. Ping Yang from the Division of Clinical Epidemiology at Mayo Clinic addressed this issue by undertaking a longitudinal evaluation of prospective patients to assess the quality of life in long-term lung cancer survivors.

Out of 2837 patients who were enrolled in the study from 1997 to 1999, 411 or 14% of these patients were actually identified as long-term survivors. During short-term (within 3 years of diagnosis) and long-term (beyond 5 years from diagnosis) follow-up, patients were asked to complete the self-administered Lung Cancer Symptom Scale questionnaire (scores 0-100 from best to worst) to assess their overall quality of life.

Changes in quality of life over time were assessed using non-parametric tests. Declining quality of life was defined as a 10 point increase or more on the LCSS from short-term to long-term follow-up. A greater than 50 point score on the LCSS indicated a poor quality of life for the patient.

Forty percent or 164 (90 men and 74 women) of the 411 long-term lung cancer survivors completed both the short-term and long-term follow-up LCSS questionnaires. The median age of these patients at diagnosis was 68 years with a range of 32 to 85. The mean quality of life score declined from 19.0 in the short term to 25.8 in the long-term follow-up ($p=0.07$) with 34% of all long-term survivors experiencing a declining quality of life over time.

Poor quality of life at long-term follow-up was more frequent in men than in women (22% vs. 11%, $p=0.05$), and 31% of patients aged 75 or older also reported poor quality of life at long-term follow-up. Diminished quality of life at the short-term follow-up was associated with administration of chemotherapy or radiation and suffering from comorbid chronic obstructive pulmonary disease ($p<0.05$).

After adjusting for age, gender, smoking history, tumor stage/histology, comorbidity, and lung cancer treatment, the occurrence of recurrent or second primary lung cancers was significantly associated with declining quality of life over time ($p=0.02$). Lung cancer stage did not accurately predict quality of life in either short-term or long-term follow-up.

When compared to other patient populations, the results show that there are substantial deficits in the quality of life of long-term lung cancer survivors. Yang and her colleagues stress the need for targeted interventions to improve the lives of these survivors.

Percutaneous Radiofrequency Ablation

Radiofrequency ablation (RFA) is a promising new technique currently used by some physicians to treat primitive and secondary neoplasms. RFA is a minimally invasive procedure whereby a small needle is inserted into the tumor and emits energy to heat and destroy cancerous cells.

Marcello Carlo Ambrogi, a thoracic surgeon from Pisa, Italy, recently conducted a study to evaluate the efficacy of RFA in the treatment of non-small cell lung cancer.

Twenty-three patients (20 males, 3 females, mean age of 74.5 years) diagnosed with primary NSCLC were included in the study. Out of the 23 patients, 16 had stage I, 2 had stage III and 5 had stage IV NSCLC. A 14 Gauge needle with 9 deployable electrodes was used to emit radiofrequency energy supplied by a generator with a max power of 150 W. The temperature was maintained for 15-27 minutes at 90°C.

No mortalities were observed, and there were 4 cases of partial pneumothorax morbidity. A 65% complete response was recorded at a mean follow-up of 20.3 months. Mean overall survival was 16.2 months, which increases to 19.6 months for stage I patients.

Based on these results, Ambrogi found RFA of lung tumors to be both feasible and safe. A number of physicians are currently using RFA when typical surgery cannot be performed. After continued follow-up studies, investigators hope that more information will be available to ultimately judge RFA's efficacy and its possible role in other applications.

Prostate Cancer:
NCI Tests Cancer Vaccine And Hormone Therapy

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either vaccine or second-line antiandrogen treatment, which consisted of the hormone nilutamide. Nilutamide works by blocking the effects of excess testosterone, a hormone produced by the body that can promote the growth of cancer cells. After the first six months of treatment, participants in both arms of the study—who had rising PSA levels but no evidence of metastatic disease—could choose to receive the other treatment in combination with their first study treatment.

There were no serious side effects from the vaccine, but some of the participants receiving nilutamide experienced severe adverse reactions involving lung toxicities, an uncommon side effect sometimes associated with the drug. Median time before the treatment started to fail was 9.9 months for individuals who received vaccine alone compared to 7.6 months for patients on nilutamide alone, a difference not considered statistically significant. However, 12 of the 21 vaccine recipients had nilutamide added to their treatment regimens after six months. The patients in that group experienced an additional median time of 13.9 months until treatment failure, for a total of 25.9 months from the beginning of their treatments.

The positive effects of combining antiandrogen therapy to vaccine "may be because the vaccine acts to 'prime' the immune system, and when you add the hormone treatment, it allowed the vaccine to work even better," explained Arlen. "Our study indicates there may well be a synergy between immunotherapy with vaccines and hormone deprivation."

The rationale for testing a vaccine/hormone therapy combination came from clinical observations showing that hormone therapy increases the number of immune cells reaching the prostate gland, thereby allowing vaccines to work more effectively.

Arlen and his NCI colleagues are planning a follow-up study using the vaccine and antiandrogen at the same time, instead of sequentially, in similar patients. They will be testing a more potent, newer prostate cancer vaccine in the next study. The NCI scientists will also use a different hormone treatment called flutamide, which has fewer and less serious side effects than nilutamide.

Two-Point Rise In PSA Signals High-Risk Prostate Cancer

Men treated with radiation therapy only—the standard therapy for men categorized with "low-risk" disease—but who also experienced a two-point rise in prostate-specific antigen during the year preceding diagnosis, had a very high death rate from prostate cancer, according to researchers from Brigham and Women's Hospital, Boston.

Men who experience this rise in PSA should be considered for RT and androgen suppression therapy (AST), the standard treatment for men with high-risk disease, the researchers said.

The study findings were published in the July 27 issue of the Journal of the American Medical Association.

Previous research spearheaded at BWH revealed that a two-point increase in PSA the year prior to radical prostatectomy (RP) signaled metastatic disease.

Currently, PSA testing helps provide evidence that the disease is present and also indicates how aggressive it is. However, guidelines are only now forming on how to best interpret PSA levels and translate them into recommendations regarding whom to biopsy and what treatment to offer. This study provides additional evidence to support the dictum that it is not the level of PSA but its change over time, specifically a rise of more than two-points in a year, that should prompt physicians to identify the cancer as having already metastasized and therefore recommend more aggressive combination treatments.

"Previous studies have found that PSA testing over time is a reliable indicator of the risk of death from prostate cancer," said the study's lead author, Anthony D'Amico, chief of Genitourinary Radiation Oncology at the BWH and Dana-Farber Cancer Institute and professor of radiation oncology at Harvard Medical School.

"This research establishes a new paradigm for PSA and takes our understanding of the biomarker to a higher level," D'Amico said. "Now, physicians planning to treat a man with RT for low-risk disease need to ensure that a two-point rise in PSA did not occur during the year prior to diagnosis. If it had, the RT and AST therapy should be strongly considered to combat the more aggressive cancer that the two-point rise in PSA is indicating."

D'Amico, who also recommends that PSA be measured at age 35 to establish a baseline (before enlargement of the prostate occurs and confounds the PSA test) assessed whether a PSA rise of more than two ng/ml during the year prior to diagnosis was significantly associated with prostate cancer-specific mortality (PCSM) following RT. Researchers evaluated PSA velocity among 358 men who were treated with RT for localized prostate cancer between 1988 and 2002.

The median age of the men at the time of initial therapy was 71 years with a median follow up of four years following RT. Patients had a serum PSA measurement approximately every 12 months and a digital rectal examination prior to diagnosis.

Overall there were 160 PSA recurrences and 79 deaths of which 30 were from prostate cancer. Of the 30 prostate cancer death observed, 28 occurred in men whose PSA rose by more than two points during the year prior to diagnosis.

Researchers found that a PSA velocity of more than two ng/ml per year was significantly associated with a shorter time to PCSM resulting in a 12-fold increase in PCSM compared to men whose PSA velocity was two ng/ml or less. This translated into nearly 20 percent of men dying of prostate cancer within seven years following RT despite low-risk disease.

Cervical Cancer:

High Cervical Cancer Rates Indicate Access Problems

High rates of cervical cancer are indicators of larger problems in access to health care, according to a report compiled by the National Cancer Institute's Center to Reduce Cancer Health Disparities.

The U.S. health care system must improve its delivery of cervical cancer education, screening, treatment, and related health care to women at risk to address burgeoning health disparities, the report concludes.

Overall, there has been a consistent decline in cervical cancer deaths in the U.S., but patterns of high cervical cancer mortality have plagued specific geographic areas and populations, including African-American women in the South, Hispanic women along the Texas-Mexico border, white women in Appalachia,

American Indians of the Northern Plains, Vietnamese American women, and Alaska Natives.

The report suggests that cervical cancer is an indicator of larger health system concerns, including medical care access, cultural issues, health communication and education issues.

The NCI's CRCHD conducted the Cervical Cancer Mortality Project to examine the underlying causes of this disparity. CRCHD found that women suffering from high cervical cancer mortality share several life conditions: they tend not to have a usual source of health care; have lower rates of preventative health services, including cancer screening; have low incomes and educational levels; and live in regions with high rates of screenable and treatable diseases, such as breast cancer, colorectal cancer, cerebrovascular disease, and infant mortality.

"Effectively addressing cervical cancer mortality can provide a model for action and an opportunity to address not only the health problems facing women who are dying from cervical cancer, but also the full set of human circumstances that lead to health disparities," said CRCHD Director Harold Freeman.

The report, "Excess Cervical Cancer Mortality: A Marker for Low Access to Health Care in Poor Communities," made the following recommendations:

—Intensify outreach to women who have rarely or never been screened for cervical, breast, or colon cancer and other screenable diseases by establishing "medical homes," a usual source of medical care where they can receive screening and counseling, experience continuity of care, and build relationships with the medical caregivers.

—Pairing all women with patient navigators at local hospitals or primary health centers, who can help at-risk women through the health system once an abnormality has been detected.

—Increasing the number of female providers, particularly those of the patient's race/ethnicity, to break down some women's resistance to screening; several women are more reluctant to receive care from male physicians due to distrust or other cultural issues.

—To improve coverage and reimbursement for cancer-related services, any uninsured woman with cervical or other cancer should be considered eligible for Medicaid or Medicare for the duration of her treatment and follow-up care.

—Working with community members to develop linguistically and culturally appropriate information about this disease and improving provider-patient communication through provider tools and broadening the availability of language translation.

—Additional research is needed to study the effects of numerous factors on cervical cancer mortality.

—All government, state, and local programs with an interest in women's health should pursue collaborations which promote a "whole woman" approach to health care.

Cancer Survivorship:
Lifestyle Changes Common After Cancer Diagnosis

An analysis of more than 100 studies of cancer survivors shows that many survivors initiate diet, exercise, and other beneficial lifestyle changes following a cancer diagnosis, but that those who are male, older, and less educated are less likely to adopt such changes.

The term "cancer survivor" refers to a person who has been diagnosed with cancer.

The review, published online July 25 in the Journal of Clinical Oncology, says that a cancer diagnosis often prompts immediate changes in health behavior, including significant modifications in diet and physical activity.

Using the MEDLINE and PubMed databases, lead author Wendy Demark-Wahnefried, of Duke University Medical Center, and colleagues from the National Cancer Institute and Brown University identified and reviewed more than 100 studies of cancer survivors published since 1996.

Researchers found that many survivors adopt healthier behaviors, such as following a healthier diet (30-60% of survivors), quitting smoking (46-96% of smokers with tobacco-related cancers, such as lung or head and neck), abstaining from alcohol (47-59% of those with head and neck cancers, which are closely linked to alcohol use), and regular physical activity (with up to 70% of survivors reporting 30 minutes of exercise a day, at least 5 days a week).

Many of these changes should be beneficial because cancer survivors are a vulnerable population, at increased risk for second cancers, osteoporosis, obesity, cardiovascular disease, and diabetes.

However, researchers noted that not all cancer patients adopted healthier behaviors, with only 25-42% of survivors consuming adequate amounts of fruits and vegetables, and roughly 70% of breast and prostate cancer survivors remaining overweight or obese.

The analysis also found conflicting data on physical activity, as well as smoking status, noting that

although survivors with tobacco- or alcohol-related cancers were more likely to reduce or eliminate these behaviors, 20% of survivors continue to smoke, a figure that is not much different from smoking status in the general population (24%).

Also, researchers found that males, less educated individuals, survivors over age 65, and those who live in urban areas were less likely to initiate or maintain healthy lifestyle changes.

The study also found that while physicians are among the most powerful catalysts for promoting behavior change, only 20% of oncologists provide such guidance because of time constraints, competing treatment or health concerns, and uncertainty regarding the delivery of health behavior messages and their potential impact on a patient's outcome.

An accompanying editorial by Patricia Ganz, of the Jonsson Comprehensive Cancer Center at the University of California, Los Angeles, and co-chairman of the ASCO Survivorship Task Force, noted that while a recent survey of ASCO members found that the majority of oncologists believe it is their role to provide ongoing medical care, "it is not yet clear how focused that care is on surveillance for cancer recurrence versus health promotion, disease prevention, and monitoring or prevention of late effects."

Ganz pointed to the transition time at the end of cancer treatment as a "teachable moment" for oncologists as well, adding, "Cancer survivors are looking for important ways to prevent a recurrence of their cancer, and to enhance the quality and length of their lives. Oncologists too are faced with a teachable moment, and have an opportunity to define what care of the cancer survivor should include, and what each survivor can expect after completing their initial curative-intent therapy."

More than 10 million cancer survivors live in the U.S. today, and an estimated 64% of those diagnosed with cancer can expect to be alive after five years, up from less than 50% in 1971.

In December 2004, ASCO formed a Survivorship Task Force, which is undertaking a range of initiatives to improve the care of cancer survivors. These initiatives may include revising the organization's oncology training curriculum and enhancing ASCO's educational programs to ensure that physicians are better prepared to address the unique needs of cancer survivors; developing clinical practice guidelines on long-term care and monitoring of cancer survivors; and supporting additional research on interventions to improve the long-term care of survivors.

Eye Cancer:

Proton Beam Radiation Helps Cancer Patients Retain Vision

Patients with cancer affecting their eye can usually avoid visual handicap, loss of the eye, and spread of the disease by receiving proton beam radiation therapy, according to a study published in the Aug. 1 issue of the International Journal of Radiation Oncology-Biology-Physics, the journal of the American Society for Therapeutic Radiology and Oncology.

The study, conducted on 349 patients in conjunction with the Liverpool Ocular Oncology Centre in the U.K., set out to determine visual acuity, local tumor control, ocular retention and overall survival after patients received proton beam radiation therapy for melanoma affecting their eyes.

The patients chosen were deemed unsuitable for other forms of treatment because of their tumor size and location, with 75 percent of the patients having tumors that extended to within three millimeters of the optic disk, which if affected can cause blindness. The large tumors also posed an increased risk of the tumor returning, retinal detachment and glaucoma.

Of the 346 patients who had the ability to count fingers before treatment began, 79.1 percent of them retained that ability at the five year mark. Before treatment, 212 patients had 20/40 vision, 44.8 percent were able to retain that visual acuity five years following radiation therapy. Overall survival rates based on the cancer spreading to other parts of the body was high with 90 percent of the patients able to stave off further disease when they were checked at the five year milestone.

"What is special is that these good results, similar to other studies, are achieved despite the fact that we reserve proton beam radiation therapy for patients who we feel would not do well with other methods," said Bertil Damato, a doctor at St. Paul's Eye Unit at Royal Liverpool University Hospital in Liverpool, England.

Cooperative Group Trials Approved By NCI Are Listed

The National Cancer Institute's Cancer Therapy Evaluation Program approved the following clinical research studies last month. For further information about a study, contact the principal investigator listed.

Phase I

Cancer Research UK Phase I Trial to Evaluate the Safety, Tolerability and Pharmacokinetics of

17-dimethylaminoethyl-amino-17-demethoxy geldanamycin (17-DMAG) Given as a Once Weekly Infusion in Patients with Advanced Solid Tumors. Royal Marsden Institute of Cancer Research, protocol 6547, Judson, Ian, phone 44-0-208-722-4302.

Phase I Study of BAY 43-9006 in Patients with Acute Leukemias, Myelodysplastic Syndromes and Chronic Myeloid Leukemia in Blast Phase. M.D. Anderson Cancer Center, protocol 6742, Cortes, Jorge Eduardo, phone 713-794-5783.

Phase I Study of Suberoylanilide Hydroxamic Acid in Combination with Bortezomib in Patients with Advanced Malignancies. University of Wisconsin Hospital and Clinics, protocol 6910, Wilding, George, phone 608-263-8610.

Phase I Study of 5-Azacitidine in Combination with Interferon-Alfa 2B in Unresectable or Metastatic Melanoma and Renal Cell Carcinoma. Yale University, protocol 7317, Sznol, Mario, phone 203-785-6221.

Phase I/II

Phase I/II Study of BMS-247550 and Pegylated Liposomal Doxorubicin in Patients with Advanced Epithelial Ovarian Cancer or Primary Peritoneal with a Platinum and a Taxane. Weill Medical College of Cornell University, protocol 7229, Chuang, Ellen, phone 212-821-0654.

Phase I/II Study of Daily Oral Polyphenon E in Asymptomatic, Rai Stage 0-II Patients with Chronic Lymphocytic Leukemia. Mayo Clinic Rochester, protocol 7303, Kay, Neil, phone 507-284-2511.

Phase I/II Trial of Intracerebral IL13-PE38QQR Infusion in Pediatric Patients with Recurrent Malignant Glioma. Pediatric Brain Tumor Consortium, protocol PBTC-011C, Banerjee, Anuradha, phone 415-353-2966.

Phase I/II Trial of a Combination of Paclitaxel and Trastuzumab with Daily Irradiation or Paclitaxel Alone with Daily Irradiation Following Transurethral Surgery for Non-Cystectomy Candidates with Muscle-Invasive Bladder Cancer. Radiation Therapy Oncology Group, protocol RTOG 0524, Michaelson, Dror, phone 617-726-1594.

Phase II

Phase II Trial of BMS 247550 in Advanced Renal Cell Carcinoma. University of Chicago, protocol 7084, Undevia, Samir, phone 773-834-8141.

Phase II Study of GM-CSF in Patients with Chronic Phase Chronic Myeloid Leukemia Who Are Not in Complete Cytogenetic Remission After Initial Therapy. Wake Forest University, protocol 7350, Molnar, Istvan, phone 336-716-4464.

Randomized Phase II Trial of Rituximab vs. Lenalidomide vs. Ritixumab + Lenalidomide in Recurrent Follicular Non-Hodgkin Lymphoma After Relapse From a Rituximab-Containing Combination Regimen. Cancer and Leukemia Group B, protocol CALGB-50401, Leonard, John, phone 212-746-2932.

Bevacizumab and CHOP in Combination for Patients with Peripheral T-Cell or Natural Killer Cell Neoplasms. Eastern Cooperative Oncology Group, protocol E2404, Ganjoo, Kristen, phone 650-493-5000.

Phase II Trial of Pemetrexed Disodium and Carboplatin in Previously Untreated Extensive Stage Small Cell Lung Cancer. North Central Cancer Treatment Group, protocol N0423, Jett, James, phone 507-538-1079.

Tandem Autologous Stem Cell Transplantation for Patients with Primary Progressive or Recurrent Hodgkin's Disease (A BMT Study), Phase II. Southwest Oncology Group, protocol S0410, Smith, Eileen, phone, 626-359-8111 ext. 63077.

Phase II Trial of BAY 43-9006 in Advanced Soft Tissue Sarcomas. Southwest Oncology Group, protocol S0505, Von Mehren, Margaret, phone 215-728-3545.

Other

Prospective Evaluation of Pelvic Exenteration in Patients with Recurrent Cervical Cancer. Gynecologic Oncology Group, protocol GOG-0222, McMeekin, Scott, phone 405-271-8707.

Establishment of a Head and Neck Cancer Tissue/Specimen Bank. Radiation Therapy Oncology Group, protocol RTOG-0514, Weber, Randal, phone 713-792-6920.

Cytogenetic and Fluorescence In Situ Hybridization Studies in Multiple Myeloma. Southwest Oncology Group, protocol SO334, Persons, Diane, phone 913-588-1728.

Molecular Epidemiology Case-Series Study of Non-Small Cell Lung Cancer in Smoking and Non-Smoking Women and Men. Southwest Oncology Group, protocol SO424, Ambrosone, Christine, phone 716-845-3082.

Pilot

Pilot Study Evaluating Surrogates of Response to Short Term Oral Suberoylanilide Hydroxamic Acid. Johns Hopkins University, protocol 6914, Stearns, Vered, phone 443-287-6489.

A Notch-Signaling Pathway Inhibitor in Patients with T-cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL)

An investigational study for children, adolescents and adults with relapsed and refractory T-cell acute lymphoblastic leukemia/lymphoma is now accruing patients at various centers around the country.

This study's goal is to evaluate the safety and tolerability of a Notch inhibitor as a rational molecular therapeutic target in T-ALL, potentially uncovering a novel treatment for these cancer patients.

Eligibility criteria and treatment schema for the study include:

Notch-Signaling Pathway Inhibitor in Patients with T-ALL	
Eligibility Criteria	Patient must be = 12 months with a diagnosis of T-cell acute lymphoblastic leukemia/lymphoma AND must also have: • Relapsed T-ALL • T-ALL refractory to standard therapy • Not be a candidate for myelosuppressive chemotherapy due to age or comorbid disease ECOG performance status =2 for patients >16 years of age OR Lanksy performance level >50 for patients 12 months to =16 years of age Fully recovered from any chemotherapy and >2 weeks from radiotherapy, immunotherapy, or systemic steroid therapy with the exception of hydroxyurea or intrathecal therapy Patient must be >2 months following bone marrow or peripheral blood stem cell transplantation No treatment with any investigational therapy during the preceding 30 days No active or uncontrolled infection
Treatment Plan	Open label and non-randomized, this study is conducted in two parts. Part I is an accelerated dose escalation to determine the maximum tolerated dose (MTD), and Part II is a cohort expansion at or below the MTD. MK-0752 will be administered orally. Plasma concentrations will be measured at defined time intervals.

For information regarding centers currently open for enrollment, please contact 1-888-577-8839.